

10/537000

Case serial number: 10/537000

Class / Subclass(es): 435/6

Earliest Priority Filing Date: French 11/28/02

Format preferred for results: E-mail

Attachment: Yes.

Search Topic Information:

I need a structure search of the elected species Y2 in claim 43 and species Y'2 in claim 44. I've attached pages from the PqPub document - US2006/0160086 - which include images of the structure itself and the examples where the structure was synthesized. (I think the structure in the claims is too faint). I've also included the relevant claims (28, 35, 43, 44) and the abstract.

10/537000

\*\*\*\*\* INVENTOR RESULTS \*\*\*\*\*

=> d his l17

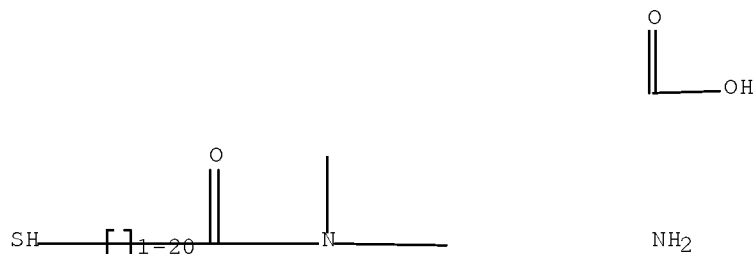
(FILE 'HCAPLUS' ENTERED AT 17:08:33 ON 19 MAR 2008)

L17 1 S ((L13-L16) AND L9) OR (L1 AND L9)

=> d que l17

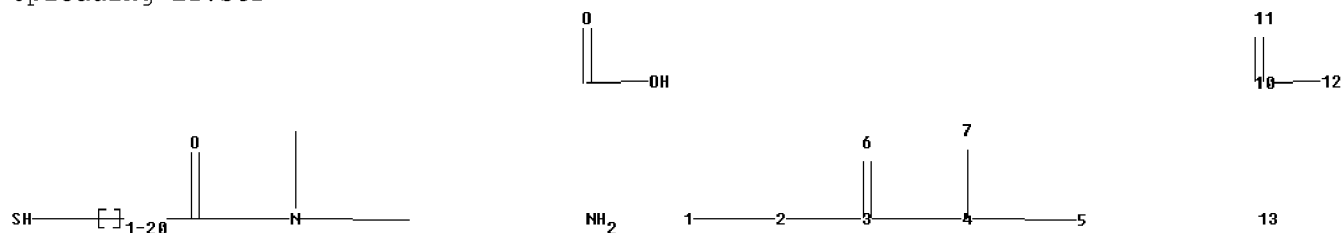
L1 1 SEA FILE=HCAPLUS ABB=ON PLU=ON US20060160086/PN

L2 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L1.str



chain nodes :

1 2 3 4 5 6 7 10 11 12 13

chain bonds :

1-2 2-3 3-4 3-6 4-5 4-7 10-11 10-12

exact/norm bonds :

1-2 3-4 3-6 4-5 4-7

exact bonds :

2-3

normalized bonds :

10-11 10-12

Match level :

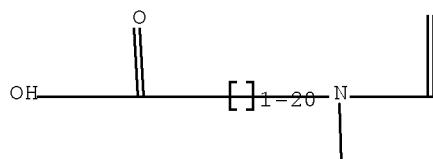
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 10:CLASS 11:CLASS

12:CLASS 13:CLASS

L4 64 SEA FILE=REGISTRY SSS FUL L2

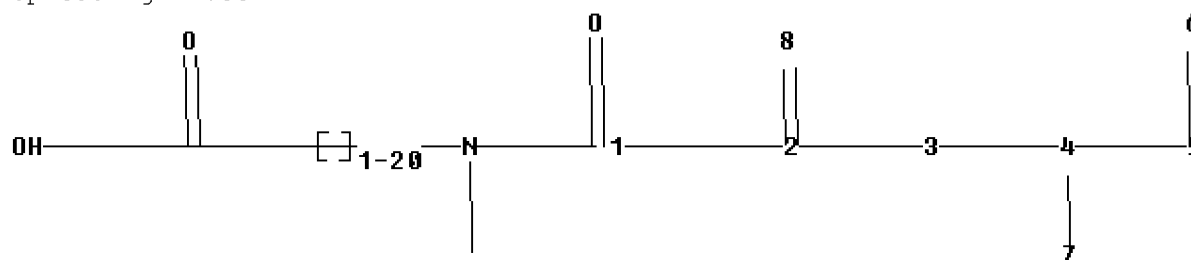
L5 STR

10/537000



Structure attributes must be viewed using STN Express query preparation:

Uploading L2.str



chain nodes :

1 2 3 4 5 6 7 8

chain bonds :

1-2 2-3 2-8 3-4 4-5 4-7 5-6

exact/norm bonds :

3-4 4-5 4-7 5-6

exact bonds :

2-3

normalized bonds :

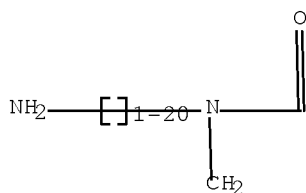
1-2 2-8

Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS

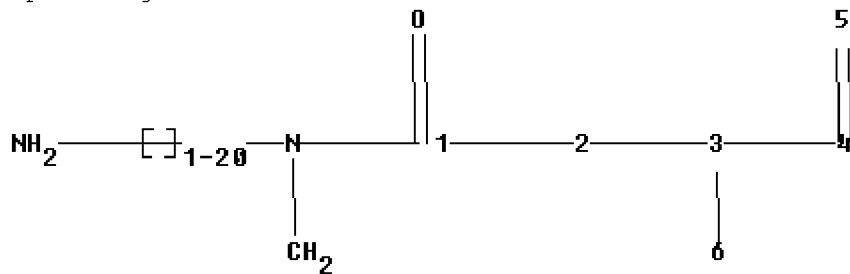
L6

STR



Structure attributes must be viewed using STN Express query preparation:

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Uploading L3.str
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Match level :  
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS

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L8      14 SEA FILE=REGISTRY SUB=L4 SSS FUL (L5 OR L6)
L9      8 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L13     51 SEA FILE=HCAPLUS ABB=ON PLU=ON VOLLAND H?/AU
L14     190 SEA FILE=HCAPLUS ABB=ON PLU=ON CREMINON C?/AU
L15     3 SEA FILE=HCAPLUS ABB=ON PLU=ON NEUBURGER L?/AU
L16     274 SEA FILE=HCAPLUS ABB=ON PLU=ON GRASSI J?/AU
L17     1 SEA FILE=HCAPLUS ABB=ON PLU=ON (((L13 OR L14 OR L15 OR L16))
AND L9) OR (L1 AND L9)

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=> dup rem 117 127
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FILE 'HCAPLUS' ENTERED AT 17:21:21 ON 19 MAR 2008  
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FILE 'PASCAL' ENTERED AT 17:21:21 ON 19 MAR 2008  
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FILE 'SCISEARCH' ENTERED AT 17:21:21 ON 19 MAR 2008  
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PROCESSING COMPLETED FOR L17  
PROCESSING COMPLETED FOR L27

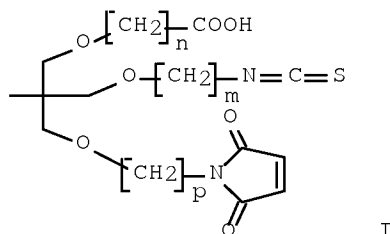
10/537000

L28 9 DUP REM L17 L27 (3 DUPLICATES REMOVED)  
 ANSWER '1' FROM FILE HCAPLUS  
 ANSWERS '2-7' FROM FILE BIOSIS  
 ANSWERS '8-9' FROM FILE PASCAL

=> d l28 1 ibib abs hitstr; d l28 ibib ab 2-9

L28 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:450626 HCAPLUS Full-text  
 DOCUMENT NUMBER: 141:33109  
 TITLE: Apparatus and process for the continuous detection of  
 an analyte using a trifunctional detection reagent  
 INVENTOR(S): Volland, Herve; Creminon, Christophe  
 ; Neuburger, Laure Marie; Grassi,  
 Jacques  
 PATENT ASSIGNEE(S): Commissariat a l'Energie Atomique, Fr.  
 SOURCE: Fr. Demande, 49 pp.  
 CODEN: FRXXBL  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2847984	A1	20040604	FR 2002-14959	20021128
CA 2506548	A1	20040617	CA 2003-2506548	20031128
WO 2004051271	A1	20040617	WO 2003-FR3521	20031128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003294102	A1	20040623	AU 2003-294102	20031128
EP 1567865	A1	20050831	EP 2003-789522	20031128
EP 1567865	B1	20061115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006508357	T	20060309	JP 2004-556436	20031128
AT 345498	T	20061215	AT 2003-789522	20031128
ES 2276149	T3	20070616	ES 2003-789522	20031128
US 2006160086	A1	20060720	US 2005-537000	20051220 <--
PRIORITY APPLN. INFO.:			FR 2002-14959	A 20021128
			WO 2003-FR3521	W 20031128
OTHER SOURCE(S):			MARPAT 141:33109	
GI				



AB An analyte (a) contained in a fluid sample, such as water or biol. fluids, is detected by (1) saturation of a solid support with a trifunctional reagent (Y) having a luminescent group (L), a mol. (B) which can be an analog or a fragment of the analyte (a), and a functional group for the fixation of the reagent to the solid support, a receptor (Q) for the analyte (a) serving as a luminescence acceptor of the group (L) by forming (C) between the mol. (B) and the receptor (Q), (2) contacting the solid support obtained in step (1) with the fluid sample containing (a), (3) measuring the fluorescence intensity of the signal emitted by the group (L) which is proportional to the concentration of (a) in the sample, and (4) regenerating the solid support by contacting the solid support with receptor (Q). Steps (3) and (4) are carried out continuously. The solid support can be made of glass, plastics, ceramics, metals, or alloys as tubes, capillaries, plates, or beads. (C) can consist of peptide, nucleotide, glucoside, or hydrocarbon chains which can contain heteroatoms, such as N, O, S, and it has three chemical reactive functional groups F1, F2, and F3. The luminescent group (L) is covalently bound to F1 of the trifunctional reagent. (B) is reversibly and noncovalently bound to the receptor (Q) and covalently bound to F2 of the trifunctional reagent. F3 of the trifunctional reagent is used for the fixation of the complex to the solid support. The groups F1, F2, and F3 can be amino groups R-NH<sub>2</sub>, R-NH-, (R)<sub>3</sub>-N, R-NH-OR, and NH<sub>2</sub>-OR, an alc. group R-OH, a halogen-containing group R-X with R representing alkyl, aryl, vinyl, or allyl groups. The luminescent group can be fluorescein, rhodamine and their derivs., DAPI, acridine, fluorescent dyes of reactive amines, BODIPY, Cascade Blue, Cy2, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, DABCYL, EDANS, eosine, erythrosine, 6-Fam, and Texas Red. The receptor can be an antibody (entire, fragment, or recombinant), a biol. receptor, nucleic acids, peptide nucleic acids, lectin, transport proteins, chelates, or synthetic receptors. The receptor has a greater affinity to (a) than to (B). The acceptor (Q) can be the same fluorescent compds. as for (L), or nonfluorescent compds., such as Black Hole Quencher 1, 2, and 3, Nanogold particles, Eclipse Dark Quencher, Elle Quencher, malachite green, the dyes QSY7, QSY9, and QSY21. (B) can be peptides, proteins, oligonucleotides, sugars, and peptide nucleic acids. The skeleton of the trifunctional reagent (Y) can have the following general structures: H<sub>2</sub>N-(CH<sub>2</sub>)<sub>m</sub>-N[(CH<sub>2</sub>)<sub>n</sub>-SH](CH<sub>2</sub>)<sub>p</sub>-COOH (Y<sub>1</sub>), H<sub>2</sub>N-(CH<sub>2</sub>)<sub>m</sub>-N[C(O)(CH<sub>2</sub>)<sub>n</sub>-SH](CH<sub>2</sub>)<sub>p</sub>-COOH (Y<sub>2</sub>), and (I) (Y<sub>3</sub>). Preferably, the skeleton of the trifunctional reagent (Y) can have the following structures: H<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>-N[(CH<sub>2</sub>)<sub>3</sub>-SH](CH<sub>2</sub>)<sub>2</sub>-COOH (Y'<sub>1</sub>), H<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>-N[C(O)(CH<sub>2</sub>)<sub>2</sub>-SH](CH<sub>2</sub>)<sub>2</sub>-COOH (Y'<sub>2</sub>), and I with n=2, m=3, and p=3 (Y'<sub>3</sub>). A The device used for the fluorescence detection of the analyte (a) can be used in lakes, rivers, swimming pools, factories, purification plants, ventilation and climate control systems.

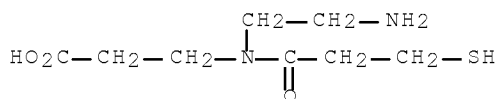
IT 697763-14-7F

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(Y'<sub>2</sub>; continuous detection of analyte using trifunctional detection reagent)

10/537000

RN 697763-14-7 HCAPLUS  
CN  $\beta$ -Alanine, N-(2-aminoethyl)-N-(3-mercapto-1-oxopropyl)- (CA INDEX  
NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN  
DUPLICATE 2

ACCESSION NUMBER: 2001:145799 BIOSIS Full-text

DOCUMENT NUMBER: PREV200100145799

TITLE: Use of free radical chemistry in an immunometric assay for  
17beta-estradiol.

AUTHOR(S): Buscarlet, Laure; Volland, Herve; Dupret-Carruel,  
Jacqueline; Jolivet, Michel; Grassi, Jacques;  
Creminon, Christophe; Taran, Frederic; Pradelles,  
Philippe [Reprint author]

CORPORATE SOURCE: Laboratoire d'Etudes Radioimmunologiques, SPI/DRM/DSV,  
CEA/Saclay, CEA, 91191, Gif-sur-Yvette Cedex, France  
philippe.pradelles@cea.fr

SOURCE: Clinical Chemistry, (January, 2001) Vol. 47, No. 1, pp.  
102-109. print.  
CODEN: CLCHAU. ISSN: 0009-9147.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Mar 2001

Last Updated on STN: 15 Feb 2002

AB Background: We wished to develop an enzyme immunometric assay for 17beta-  
estradiol (E2) in human serum using solid-phase immobilized epitope  
immunoassay (SPIE-IA) technology and free radical chemistry. Methods: We used  
an anti-estradiol monoclonal antibody as capture antibody and Fenton-like  
reagents to cross-link it to E2. The same antibody, labeled with  
acetylcholinesterase, was used for detection. Serum was diluted 10-fold before  
assay. Results: After correction by the dilution factor, the detection limit  
was 5 ng/L for human serum and intra- and interassay CVs were <7% and 15%,  
respectively, at concentrations of 169-2845 ng/L. No cross-reactivity was  
seen with other natural steroids. In comparison with a competitive commercial  
RIA performed on 88 undiluted human sera, the slope (SD) of the regression  
line was 1.05 (+/- 0.02) and the intercept was 47 (+/-27) ng/L (Sy/x = 186 ng/L)  
at concentrations of 20-5000 ng/L (r<sup>2</sup> = 0.97). Conclusions: The use of  
Fenton-like chemistry in SPIE-IA technology allows a sensitive measurement of  
E2 in human serum and could be a new approach for the development of sensitive  
immunoassays.

L28 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:472617 BIOSIS Full-text

DOCUMENT NUMBER: PREV200000472617

TITLE: Quantitative measurement of bitagged recombinant proteins

using an immunometric assay: Application to an anti-substance P recombinant antibody.

AUTHOR(S): Boquet, Didier [Reprint author]; Creminon, Christophe; Clement, Gilles; Frobert, Yveline; Nevers, Marie-Claire; Essono, Sosthene; Grassi, Jacques

CORPORATE SOURCE: Service de Pharmacologie et d'Immunologie, DRM/DSV, CEA-Saclay, 91191, Gif sur Yvette Cedex, France

SOURCE: Analytical Biochemistry, (September 10, 2000) Vol. 284, No. 2, pp. 221-230. print.  
CODEN: ANBCA2. ISSN: 0003-2697.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 1 Nov 2000  
Last Updated on STN: 10 Jan 2002

AB We have developed two different immunometric assays to directly quantify both the total and the active fractions of a recombinant antibody (single chain fragment variable, or ScFv) as obtained in a crude extract from an Escherichia coli expression system. For total determination, the assay is based on the simultaneous recognition of two different peptide Tag sequences (Ha-Tag and Myc-Tag) at each of the N- and C-terminal extremities of the recombinant protein. A monoclonal antibody (mAb 12CA5, directed against Ha-Tag), coated on microtiter plates, is used for capture, and the mAb 9E10 (directed against Myc-Tag), labeled with acetylcholinesterase (AChE, EC 3.1.1.7), acts as tracer. In parallel, for the determination of the active fraction, the capture is performed using microtiter plates coated with the antigen, while solid-phase-immobilized ScFv is measured using the same 9E10 tracer mAb. A synthetic peptide in which the two Tag sequences were joined was used as a standard, thus avoiding the laborious purification of a recombinant protein as reference. The method was applied to the direct measurement, in periplasmic extracts, of the total and active fractions of an ScFv produced at different induction temperatures.

L28 ANSWER 4 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:44879 BIOSIS Full-text

DOCUMENT NUMBER: PREV200000044879

TITLE: A solid-phase immobilized epitope immunoassay (SPIE-IA) permitting very sensitive and specific measurement of angiotensin II in plasma.

AUTHOR(S): Volland, Herve; Pradelles, Philippe; Ronco, Pierre; Azizi, Michel; Simon, Dominique; Creminon, Christophe; Grassi, Jacques [Reprint author]

CORPORATE SOURCE: Service de Pharmacologie et d'Immunologie, Departement de Recherche Medicale, CEA, CE Saclay, Batiment 136, 91191, Gif sur Yvette Cedex, France

SOURCE: Journal of Immunological Methods, (Aug. 31, 1999) Vol. 228, No. 1-2, pp. 37-47. print.  
CODEN: JIMMBG. ISSN: 0022-1759.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Jan 2000  
Last Updated on STN: 31 Dec 2001

AB We have developed a new enzyme immunometric assay for angiotensin II (AII) based on SPIE-IA technology (solid-phase immobilized epitope-immunoassay). A monoclonal antibody with optimal properties (mAb3 131) was selected from a series of 19 anti-AII mAbs. The mAb had to be purified from ascitic fluid in a specific manner in order to remove endogenous AII from the antibody-binding sites. We established a sensitive (minimum detectable concentration 0.5 pg/ml) and precise (CV below 15% in the 2-100 pg/ml range) SPIE-IA. Using different AII-related peptides, we observed that this new assay has a



specificity profile that compares favourably with the corresponding competitive immunoassay. We have used the assay to measure AII in 42 plasma samples, and demonstrated a good correlation with values obtained using a commercial radioimmunoassay. Assay specificity was supported by HPLC fractionation experiments, confirming the absence of interference induced by endogenous AII-related products.

L28 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN  
 ACCESSION NUMBER: 1996:509231 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV199699231587  
 TITLE: Two different approaches for developing immunometric assays of haptens.  
 AUTHOR(S): Grassi, Jacques [Reprint author]; Creminon, Christophe; Frobert, Yveline; Etienne, Emmanuelle; Ezan, Eric; Volland, Herve; Pradelles, Philippe  
 CORPORATE SOURCE: CEA, Serv. Pharmacol. d'Immunol., DRM, CE/Saclay, 91191 Gif sur Yvette Cedex, France  
 SOURCE: Clinical Chemistry, (1996) Vol. 42, No. 9, pp. 1532-1536. CODEN: CLCHAU. ISSN: 0009-9147.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 14 Nov 1996  
 Last Updated on STN: 14 Nov 1996

AB To improve immunoassays of small haptens, we developed two different approaches for their measurement in a noncompetitive format. We first devised two-site immunometric assays for small peptides (8-11 amino acids) by selecting two sets of antibodies specifically directed against C- and N-terminal moieties of the peptides. In each case, assay sensitivity improved substantially over that of the corresponding competitive assays. More interestingly, all of these new immunometric assays were much more specific than the competitive assays. In a second approach, we developed a new procedure, solid-phase-immobilized epitope immunoassay (SPIE-IA), in which a single monoclonal antibody uses the same epitope for capture and tracer binding and the hapten is covalently cross-linked to solid-phase proteins. To date, SPIE-IA have been successfully applied to the determination of haptens bearing primary amino groups, including substance P, thyroxine, leukotriene C4, endothelin, and angiotensin II. In each case, assay sensitivity was significantly improved.

L28 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN  
 ACCESSION NUMBER: 1997:66110 BIOSIS Full-text  
 DOCUMENT NUMBER: PREV199799365313  
 TITLE: Preferential labeling of alpha-amino N-terminal groups in peptides by biotin: Application to the detection of specific anti-peptide antibodies by enzyme immunoassays.  
 AUTHOR(S): Selo, I. [Reprint author]; Negroni, L.; Creminon, C.; Grassi, J.; Wal, J. M.  
 CORPORATE SOURCE: Lab. Assoc. INRA-CEA Immuno Allergie Alimentaire, SPI Bat 136, CE-Saclay, 91191 Gif sur Yvette Cedex, France  
 SOURCE: Journal of Immunological Methods, (1996) Vol. 199, No. 2, pp. 127-138. CODEN: JIMMBG. ISSN: 0022-1759.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 11 Feb 1997  
 Last Updated on STN: 11 Feb 1997

AB Experimental conditions (pH 6.5, 24 h reaction, peptide:biotin ratio 1:5) were defined for preferential incorporation of the biotin molecule in the N-

terminal alpha-amino group of peptides. This strategy could be helpful in numerous applications when an entire peptide chain must remain accessible for antibody or receptor binding. We illustrate this advantage in a solid-phase enzyme immunoassay designed to detect antibodies specific for bovine beta-lactoglobulin present in rabbit or human sera. This test involves synthetic peptides biotinylated in different positions and immobilized on a solid phase. The use of biotin/streptavidin interactions permitted more efficient detection of specific anti-peptide antibodies than solid phases prepared using conventional passive-adsorption techniques. The highest levels of antibody binding were measured when biotinylation occurred at the N-terminal extremity of immobilized peptides.

L28 ANSWER 7 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:157585 BIOSIS Full-text

DOCUMENT NUMBER: PREV199598171885

TITLE: Immunological studies of human constitutive cyclooxygenase (COX-1) using enzyme immunometric assay.

AUTHOR(S): Creminon, Christophe [Reprint author]; Frobert, Yveline; Habib, Aida; Maclouf, Jacques; Pradelles, Philippe; Grassi, Jacques

CORPORATE SOURCE: CEA, Serv. Pharmacol. d'Immunol., DRIPP, Cent. d'Etudes SACLAY, 91191 Gif-sur-Yvette Cedex, France

SOURCE: Biochimica et Biophysica Acta, (1995) Vol. 1254, No. 3, pp. 333-340.

CODEN: BBACAQ. ISSN: 0006-3002.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 11 Apr 1995

Last Updated on STN: 23 May 1995

AB Polyclonal antisera and six distinct monoclonal antibodies (mAbs) were raised against constitutive cyclooxygenase (COX-1) purified from ram seminal vesicles. Immunoblotting experiments revealed that the polyclonal antisera and 4 of the mAbs strongly recognized human COX in platelet extracts. Different two-site immunometric assays of ram COX-1 were established using different combinations of mAbs. The assays were performed in 96-well microliter plates coated with one mAb, with another mAb (covalently labeled with acetylcholinesterase (AChE)) as tracer. One combination (solid phase CX-101 + CX-105-AChE) exhibited the best sensitivity, with significant detection of concentrations as low as 23 pg/ml (0.3 fmol/ml of sheep COX-1). Unfortunately, this assay poorly cross-reacted with human COX-1 from platelet extracts. Another combination (solid phase CX-111 + CX-110-AChE) exhibited good recognition of human COX-1 but poor cross-reactivity with ram COX-1. Finally, purified anti-COX-1 IgG coated and CX-110-AChE were chosen as the best compromise since both good sensitivity (limit of detection, 113 pg/ml of ram COX-1) and significant cross-reactivity between COX-1 from both species were observed. In parallel, polyclonal antibodies were raised in rabbits against a peptide of 12 amino acids corresponding to the aminoterminal part of human COX-1. These polyclonal antibodies were affinity-purified and used in development of another two-site immunometric assay of COX-1 with CX-110-AChE as tracer. These two assays were used to analyze the COX-1 content of human platelets and cultured human umbilical vein cells (HUVEC). The results obtained with each assay were compared in terms of sensitivity and specificity. The validity of both assays was checked by analyzing platelets and HUVEC extracts previously fractionated by molecular sieve chromatography.

L28 ANSWER 8 OF 9 PASCAL COPYRIGHT 2008 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 1

ACCESSION NUMBER: 2005-0203414 PASCAL Full-text

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TITLE (IN ENGLISH): Solid-phase immobilized tripod for fluorescent renewable immunoassay. A concept for continuous monitoring of an immunoassay including a regeneration of the solid phase

AUTHOR: VOLLAND Herve; NEUBURGER Laure-Marie; SCHULTZ Emmanuelle; GRASSI Jacques; PERRAUT Francois; CREMINON Christophe

CORPORATE SOURCE: CEA, Laboratoire des Systemes de Lecture pour la Biologie, LETI/DSIS/SSBS/SLB, 17 Avenue des Martyrs, 38054 Grenoble, France; CEA, Laboratoire d'Etudes et de Recherche en Immunoanalyse, DRM/SPI, Batiment 136, CEA-Saclay, 91191 Gif sur Yvette, France

SOURCE: Analytical chemistry : (Washington, DC), (2005), 77(6), 1896-1904, 33 refs.  
ISSN: 0003-2700 CODEN: ANCHAM

DOCUMENT TYPE: Journal

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: United States

LANGUAGE: English

AVAILABILITY: INIST-120B, 354000125086860480

AB A new concept of immunoassay based on the use of a trifunctional reagent (tripod) and fluorescence resonance energy transfer (FRET) phenomenon is described. This procedure involves differential steps: (1) the tripod bearing (i) a fluorophore, (ii) a molecule structurally close to the target, and (iii) a linker reacts with the solid phase; (2) the solid phase is further activated with an anti-target antibody labeled with a quencher molecule, generating the decrease of the fluorophore emission via FRET; (3) FRET being distance dependent, the presence of the target by competing with the tripod for binding the quencher-labeled antibody leads to a rise of the fluorescence signal; (4) the solid phase is reactivated simply, by adding the quencher-labeled antibody. This method was evaluated in microtiter plates using the substance P as model while fluorescein and TAMRA were used as donor and acceptor, respectively. Results clearly illustrated the interest of the method, by allowing (i) a simple regeneration procedure, without requiring any drastic treatment, (ii) a direct fluorescence measurement onto the solid support, leading to a localized and cumulative signal, (iii) an increase of the signal when detecting the target, unlike classical competitive immunoassays, and (iv) a real-time monitoring of the competition and regeneration steps.

L28 ANSWER 9 OF 9 PASCAL COPYRIGHT 2008 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005-0000296 PASCAL Full-text

COPYRIGHT NOTICE: Copyright .COPYRGT. 2005 INIST-CNRS. All rights reserved.

TITLE (IN ENGLISH): Recent developments for SPIE-IA, a new sandwich immunoassay format for very small molecules  
Solid Phase Assays for Molecules with Biopharmaceuticals Importance

AUTHOR: VOLLAND Herve; PRADELLES Philippe; TARAN Frederic; BUSCARLET Laure; CREMINON Christophe KARAMANOS Nikos K. (ed.)

CORPORATE SOURCE: CEA, Service de Pharmacologie et d'Immunologie, DRM/DSV, CEA/Saclay, 91191 Gif-sur-Yvette, France; CEA, Service des Molecules Marquees et de Chimie Bioorganique, DBJC/DSV, CEA/Saclay, 91191 Gif-sur-Yvette, France; R&D Department, Technical

10/537000

Center, Diffchamb SA, 8 rue St Jean de Dieu, 69007  
Lyon, France  
Department of Chemistry, University of Patras, 261 10  
Patras, Greece

SOURCE: Journal of pharmaceutical and biomedical analysis,  
(2004), 34(4), 737-752, 51 refs.

ISSN: 0731-7085 CODEN: JPBADA

DOCUMENT TYPE: Journal

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: Netherlands

LANGUAGE: English

AVAILABILITY: INIST-19962, 354000116928380020

AB Recent publications describing new elegant approaches to assay small analytes using noncompetitive format were briefly reviewed. Among these methods, we have developed a new protocol, named SPIE-IA, which involves a cross-linking step achieved using chemical homobifunctional reagents, UV irradiation or free radicals. This new method proved to be useful to detect naturally occurring analyte-antibody complexes or to protect the analytes against degradation by peptidases. On the other hand, SPIE-IA could allow to study the adverse biological effects of UV and some aspects of free radical chemistry or to evaluate the antioxidant activity of molecules.

10/537000

\*\*\*\*\* QUERY RESULTS \*\*\*\*\*

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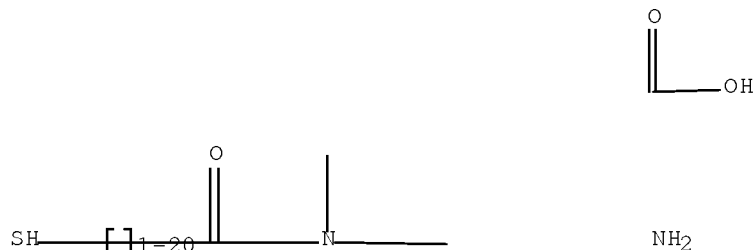
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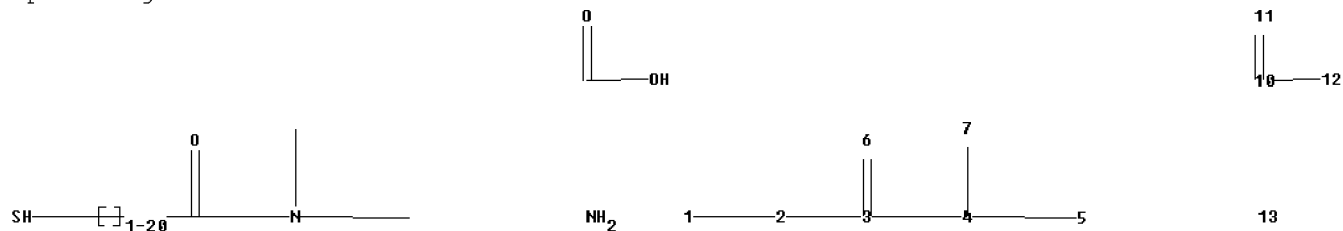
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L2 STR



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Uploading L1.str



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exact bonds :

2-3

normalized bonds :

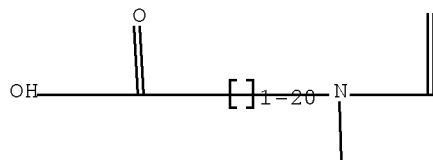
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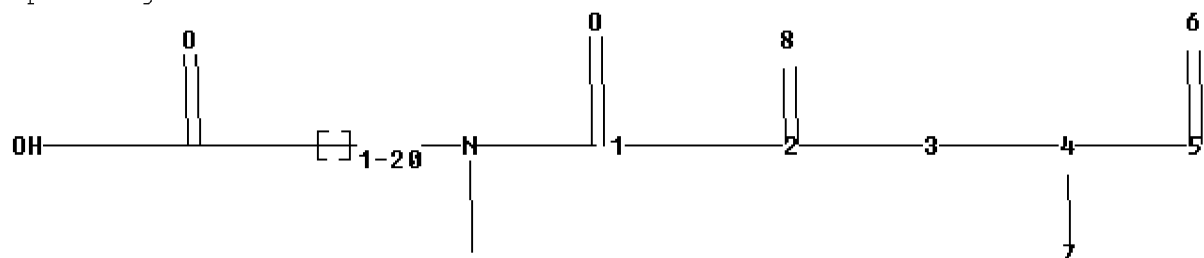
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L5 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L2.str



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exact/norm bonds :

3-4 4-5 4-7 5-6

exact bonds :

2-3

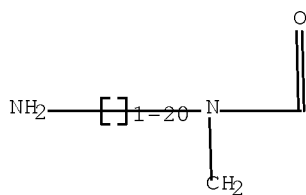
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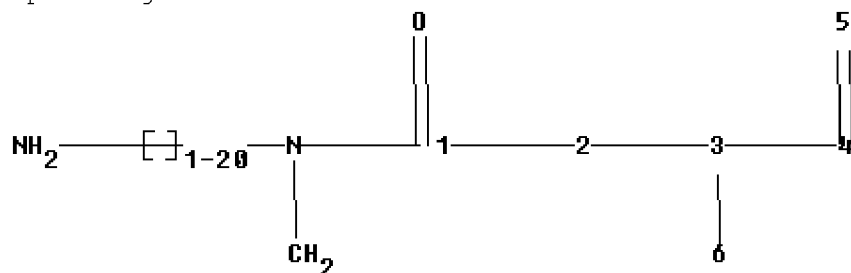
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L6 STR



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 exact/norm bonds :  
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 exact bonds :  
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Match level :  
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 L9 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L8

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L9 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2004:450626 HCAPLUS Full-text  
 DOCUMENT NUMBER: 141:33109  
 TITLE: Apparatus and process for the continuous detection of  
 an analyte using a trifunctional detection reagent  
 INVENTOR(S): Volland, Herve; Creminon, Christophe; Neuburger, Laure  
 Marie; Grassi, Jacques  
 PATENT ASSIGNEE(S): Commissariat a l'Energie Atomique, Fr.  
 SOURCE: Fr. Demande, 49 pp.  
 CODEN: FRXXBL  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2847984	A1	20040604	FR 2002-14959	20021128
CA 2506548	A1	20040617	CA 2003-2506548	20031128
WO 2004051271	A1	20040617	WO 2003-FR3521	20031128

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,  
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
 LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,  
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

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TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
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AU 2003294102 A1 20040623 AU 2003-294102 20031128  
 EP 1567865 A1 20050831 EP 2003-789522 20031128  
 EP 1567865 B1 20061115

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
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JP 2006508357 T 20060309 JP 2004-556436 20031128  
 AT 345498 T 20061215 AT 2003-789522 20031128  
 ES 2276149 T3 20070616 ES 2003-789522 20031128  
 US 2006160086 A1 20060720 US 2005-537000 20051220

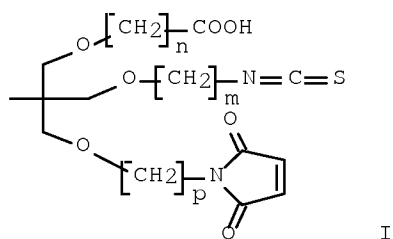
PRIORITY APPLN. INFO.:

FR 2002-14959 A 20021128  
 WO 2003-FR3521 W 20031128

OTHER SOURCE(S): MARPAT 141:33109

ED Entered STN: 04 Jun 2004

GI



AB An analyte (a) contained in a fluid sample, such as water or biol. fluids, is detected by (1) saturation of a solid support with a trifunctional reagent (Y) having a luminescent group (L), a mol. (B) which can be an analog or a fragment of the analyte (a), and a functional group for the fixation of the reagent to the solid support, a receptor (Q) for the analyte (a) serving as a luminescence acceptor of the group (L) by forming (C) between the mol. (B) and the receptor (Q), (2) contacting the solid support obtained in step (1) with the fluid sample containing (a), (3) measuring the fluorescence intensity of the signal emitted by the group (L) which is proportional to the concentration of (a) in the sample, and (4) regenerating the solid support by contacting the solid support with receptor (Q). Steps (3) and (4) are carried out continuously. The solid support can be made of glass, plastics, ceramics, metals, or alloys as tubes, capillaries, plates, or beads. (C) can consist of peptide, nucleotide, glucoside, or hydrocarbon chains which can contain heteroatoms, such as N, O, S, and it has three chemical reactive functional groups F1, F2, and F3. The luminescent group (L) is covalently bound to F1 of the trifunctional reagent. (B) is reversibly and noncovalently bound to the receptor (Q) and covalently bound to F2 of the trifunctional reagent. F3 of the trifunctional reagent is used for the fixation of the complex to the solid support. The groups F1, F2, and F3 can be amino groups R-NH<sub>2</sub>, R-NH-, (R)<sub>3</sub>-N, R-NH-OR, and NH<sub>2</sub>-OR, an alc. group R-OH, a halogen-containing group R-X with R representing alkyl, aryl, vinyl, or allyl groups. The luminescent group can be fluorescein, rhodamine and their derivs., DAPI, acridine, fluorescent dyes



of reactive amines, BODIPY, Cascade Blue, Cy2, Cy3, Cy3.5, Cy5, Cy5.5, Cy7, DABCYL, EDANS, eosine, erythrosine, 6-Fam, and Texas Red. The receptor can be an antibody (entire, fragment, or recombinant), a biol. receptor, nucleic acids, peptide nucleic acids, lectin, transport proteins, chelates, or synthetic receptors. The receptor has a greater affinity to (a) than to (B). The acceptor (Q) can be the same fluorescent compds. as for (L), or nonfluorescent compds., such as Black Hole Quencher 1, 2, and 3, Nanogold particles, Eclipse Dark Quencher, Elle Quencher, malachite green, the dyes QSY7, QSY9, and QSY21. (B) can be peptides, proteins, oligonucleotides, sugars, and peptide nucleic acids. The skeleton of the trifunctional reagent (Y) can have the following general structures: H<sub>2</sub>N-(CH<sub>2</sub>)<sub>m</sub>-N[(CH<sub>2</sub>)<sub>n</sub>-SH](CH<sub>2</sub>)<sub>p</sub>-COOH (Y<sub>1</sub>), H<sub>2</sub>N-(CH<sub>2</sub>)<sub>m</sub>-N[C(O)(CH<sub>2</sub>)<sub>n</sub>-SH](CH<sub>2</sub>)<sub>p</sub>-COOH (Y<sub>2</sub>), and (I) (Y<sub>3</sub>). Preferably, the skeleton of the trifunctional reagent (Y) can have the following structures: H<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>-N[(CH<sub>2</sub>)<sub>3</sub>-SH](CH<sub>2</sub>)<sub>2</sub>-COOH (Y'<sub>1</sub>), H<sub>2</sub>N-(CH<sub>2</sub>)<sub>2</sub>-N[C(O)(CH<sub>2</sub>)<sub>2</sub>-SH](CH<sub>2</sub>)<sub>2</sub>-COOH (Y'<sub>2</sub>), and I with n=2, m=3, and p=3 (Y'<sub>3</sub>). A The device used for the fluorescence detection of the analyte (a) can be used in lakes, rivers, swimming pools, factories, purification plants, ventilation and climate control systems.

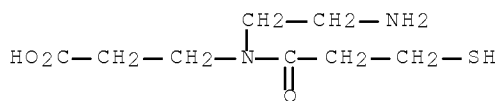
IT 697763-14-7P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(Y'<sub>2</sub>; continuous detection of analyte using trifunctional detection reagent)

RN 697763-14-7 HCAPLUS

CN β-Alanine, N-(2-aminoethyl)-N-(3-mercapto-1-oxopropyl)- (CA INDEX NAME)



IC ICM G01N033-58

ICS C07K017-00

CC 80-6 (Organic Analytical Chemistry)

Section cross-reference(s): 9, 59, 61, 73

IT 697763-14-7P

RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(Y'<sub>2</sub>; continuous detection of analyte using trifunctional detection reagent)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:353017 HCAPLUS Full-text

DOCUMENT NUMBER: 129:40146

TITLE: Detection of antagonist-dependent GPIIb/IIIa receptor antibodies

INVENTOR(S): Bednar, Bohumil; Gould, Robert J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Bednar, Bohumil; Gould, Robert J.

SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

10/537000

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822821	A1	19980528	WO 1997-US20954	19971117
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2271684	A1	19980528	CA 1997-2271684	19971117
EP 939900	A1	19990908	EP 1997-947553	19971117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001504584	T	20010403	JP 1998-523783	19971117
PRIORITY APPLN. INFO.:				
			US 1996-31661P	P 19961121
			US 1997-35461P	P 19970114
			GB 1997-2822	A 19970212
			GB 1997-5856	A 19970321
			WO 1997-US20954	W 19971117

ED Entered STN: 11 Jun 1998

AB The present invention is a method for identifying a patient at risk to developing fibrinogen receptor antagonist-induced thrombocytopenia. The method comprises incubating patient plasma with a GPIIb/IIIa receptor:GPIIb/IIIa receptor antagonist complex to form a GPIIb/IIIa receptor:GPIIb/IIIa receptor antagonist:plasma antibody complex, incubating the GPIIb/IIIa receptor:GPIIb/IIIa receptor antagonist:plasma antibody complex with a secondary anti-human detectable antibody to form a GPIIb/IIIa receptor:GPIIb/IIIa receptor antagonist:plasma antibody:secondary anti-human detectable antibody complex, and detecting the presence of the secondary anti-human detectable antibody in the GPIIb/IIIa receptor:GPIIb/IIIa receptor antagonist:plasma antibody:secondary anti-human detectable antibody complex.

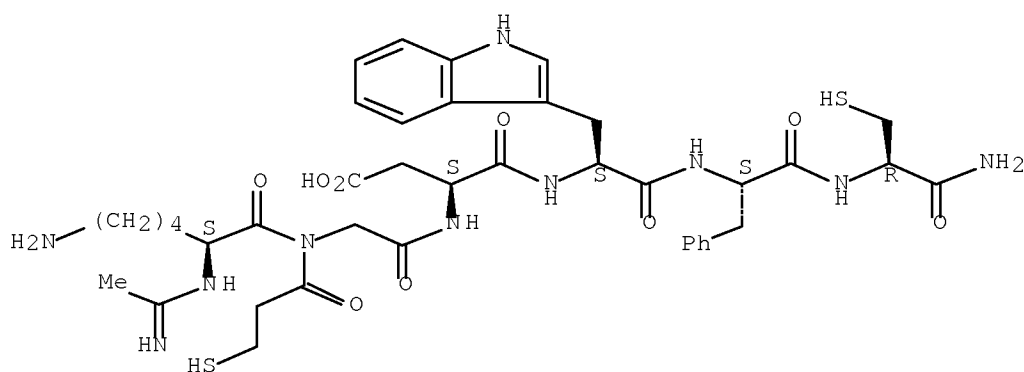
IT 197392-29-3 197392-30-6 197392-31-7  
 197392-32-8

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (detection of antagonist-dependent GPIIb/IIIa receptor antibodies for diagnosis of fibrinogen receptor antagonist-induced thrombocytopenia)

RN 197392-29-3 HCAPLUS

CN L-Cysteinamide, N2-(1-iminoethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 197392-30-6 HCAPLUS

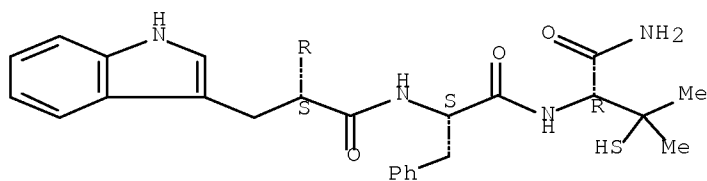
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10/537000

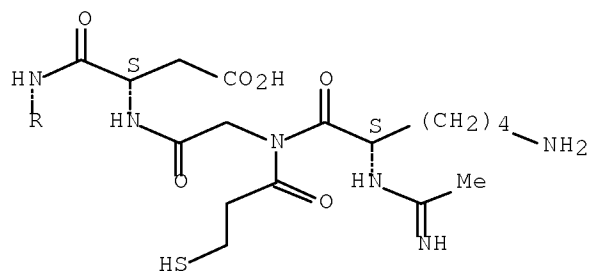
$\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

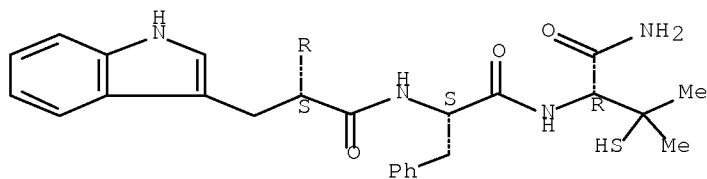


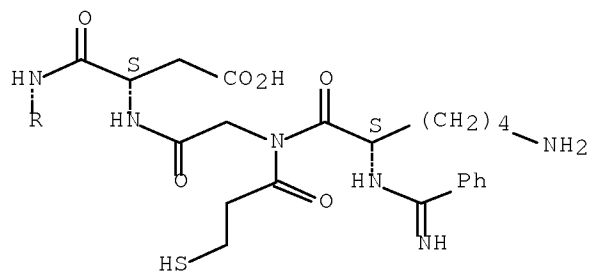
RN 197392-31-7 HCAPLUS

CN L-Valinamide, N2-(iminophenylmethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

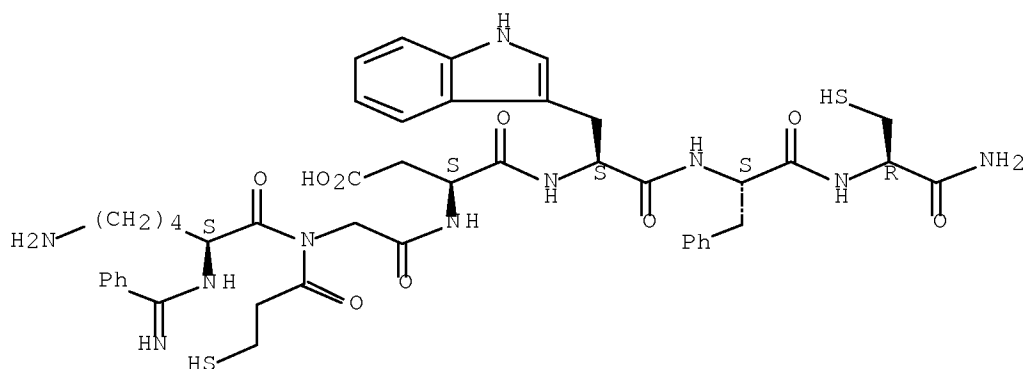
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RN 197392-32-8 HCAPLUS  
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 (CA INDEX NAME)

Absolute stereochemistry.



IC ICM G01N033-53  
 ICS G01N033-567  
 CC 15-3 (Immunochemistry)  
 IT 105806-65-3 142373-60-2 144412-49-7 169237-80-3 176022-59-6  
 197392-29-3 197392-30-6 197392-31-7  
 197392-32-8 208260-66-6  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (detection of antagonist-dependent GPIIb/IIIa receptor antibodies for  
 diagnosis of fibrinogen receptor antagonist-induced thrombocytopenia)  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1997:655453 HCAPLUS Full-text  
 DOCUMENT NUMBER: 127:303338  
 TITLE: Composition and method for reducing the risk of acute  
 coronary ischemic syndrome  
 INVENTOR(S): Gould, Robert J.; Hartman, George D.; Nichtberger,  
 Steven A.  
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Gould, Robert J.; Hartman,  
 George D.; Nichtberger, Steven A.

10/537000

SOURCE: PCT Int. Appl., 33 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735615	A1	19971002	WO 1997-US4739	19970324
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9722196	A	19971017	AU 1997-22196	19970324
PRIORITY APPLN. INFO.:				
			US 1996-14216P	P 19960327
			GB 1996-7513	A 19960411
			WO 1997-US4739	W 19970324

ED Entered STN: 15 Oct 1997

AB In patients at risk for acute coronary ischemic syndrome during angioplasty, the risk is reduced by administering a combination of a platelet glycoprotein IIb/IIIa (fibrinogen receptor) antagonist and a platelet integrin  $\alpha v \beta 3$  (vitronectin receptor) antagonist. The combination can prevent platelet thrombosis, thromboembolism, and reocclusion after angioplasty or coronary artery bypass procedures, and is also useful in treatment of unstable angina and prevention of myocardial infarction. Thus, patients with acute coronary ischemic syndrome who had received coronary revascularization with angioplasty, aspirin (325 mg/day), and heparin by i.v. bolus were administered the glycoprotein IIb/IIIa antagonist, tirofiban, and the integrin  $\alpha v \beta 3$  antagonist, 7-[[[(6-amino-2-pyridinyl)amino]carbonyl]-4-methyl-3-oxo- 2,3,4,5-tetrahydro-1H-1,2-benzodiazepine-2-acetic acid in amts. sufficient to achieve plasma levels of 40-60 ng/mL and 40-60 ng/mL, resp., for 24 h following angioplasty. Tablet and i.v. formulations of the above combination are described.

IT 197392-29-3 197392-30-6 197392-31-7  
 197392-32-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

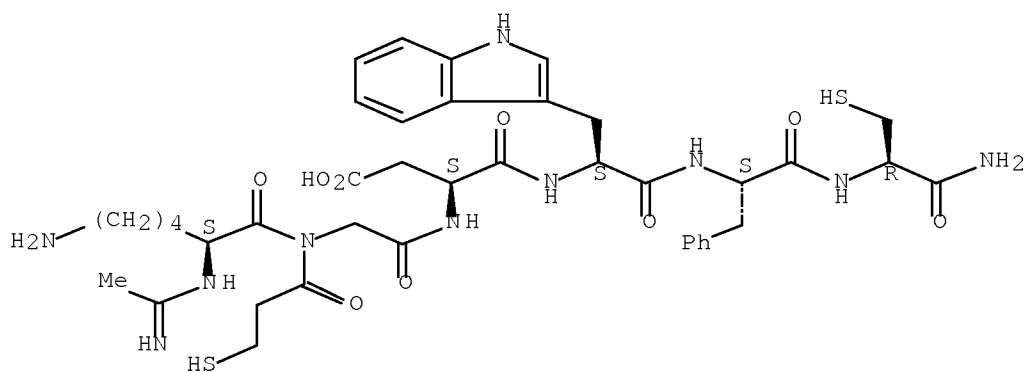
(glycoprotein IIb/IIIa antagonist; composition and method for reducing risk of acute coronary ischemic syndrome)

RN 197392-29-3 HCAPLUS

CN L-Cysteinamide, N2-(1-iminoethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/537000

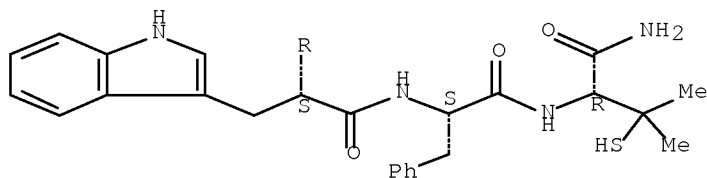


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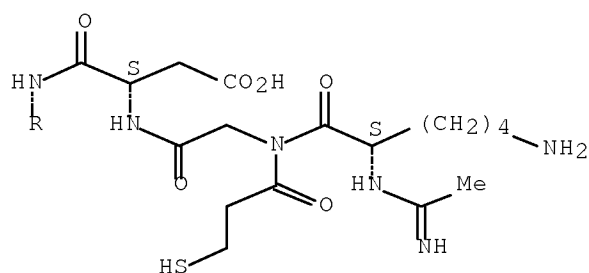
CN L-Valinamide, N2-(1-iminoethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



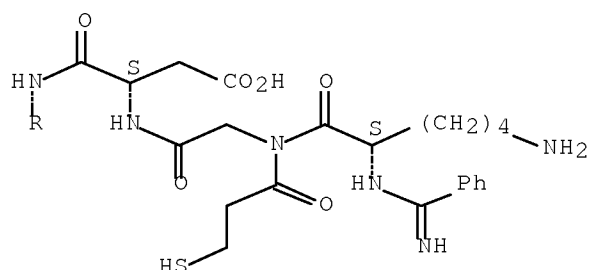
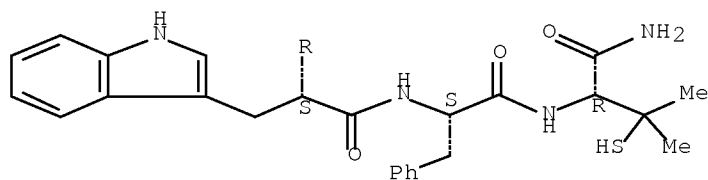
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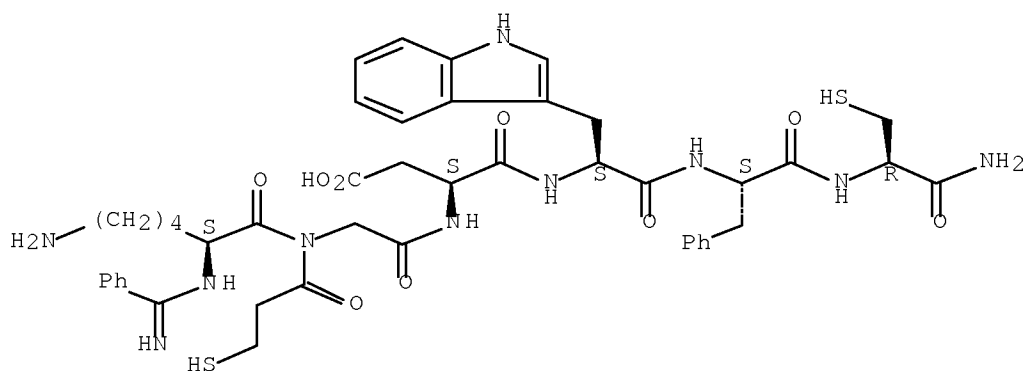
CN L-Valinamide, N2-(iminophenylmethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN	197392-32-8	HCAPLUS
CN	L-Cysteinamide, N2-(iminophenylmethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl- (9CI) (CA INDEX NAME)	

Absolute stereochemistry.



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IC      ICM  A61K039-395
CC      1-8 (Pharmacology)
        Section cross-reference(s): 63
IT      105806-65-3    142373-60-2, Tirofiban hydrochloride    144412-49-7
        169237-80-3 197392-29-3 197392-30-6
        197392-31-7 197392-32-8    197521-03-2    197521-04-3
        RL: BAC (Biological activity or effector, except adverse); BSU (Biological
        study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (Uses)

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10/537000

(glycoprotein IIb/IIIa antagonist; composition and method for reducing risk of acute coronary ischemic syndrome)

L9 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1997:650267 HCAPLUS Full-text  
DOCUMENT NUMBER: 127:303337  
TITLE: Method for inhibiting platelet aggregation and clot formation  
INVENTOR(S): Gould, Robert J.  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Gould, Robert J.  
SOURCE: PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735579	A1	19971002	WO 1997-US4631	19970324
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9723409	A	19971017	AU 1997-23409	19970324
PRIORITY APPLN. INFO.:			US 1996-14217P	P 19960327
			GB 1996-7512	A 19960411
			WO 1997-US4631	W 19970324

ED Entered STN: 13 Oct 1997

AB Platelet aggregation is inhibited, in a patient in need thereof, by administering, for a period of time >24 h, a glycoprotein IIb/IIIa receptor antagonist in an amount sufficient to achieve a steady-state plasma level which provides  $\geq 70$  % inhibition of fibrinogen binding to the IIb/IIIa receptor. This treatment reduces the risk of acute coronary ischemic syndrome during angioplasty. It may be used in combination with treatments with other anticoagulants, thrombolytic agents, and platelet aggregation inhibitors. A suitable agent is tirofiban in an amount sufficient to maintain a plasma level of 40-60 ng/mL for 24-36 h following angioplasty, administered i.v. or orally.

IT 197392-29-3 197392-30-6 197392-31-7  
197392-32-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

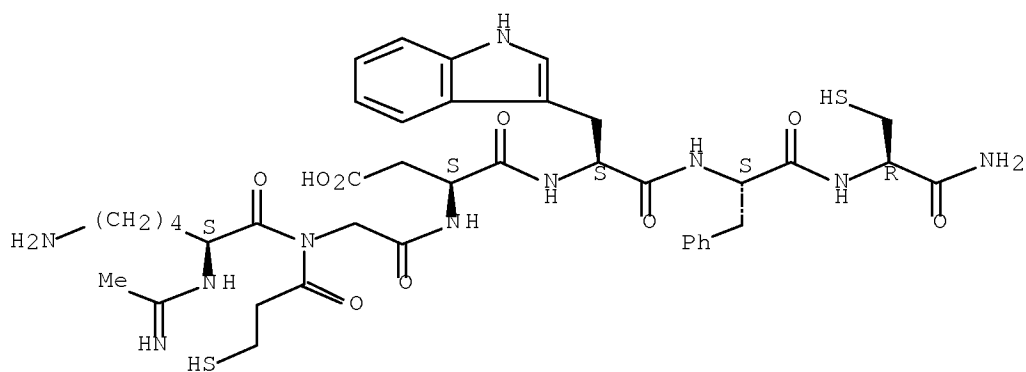
(method for inhibiting platelet aggregation and clot formation)

RN 197392-29-3 HCAPLUS

CN L-Cysteinamide, N2-(1-iminoethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



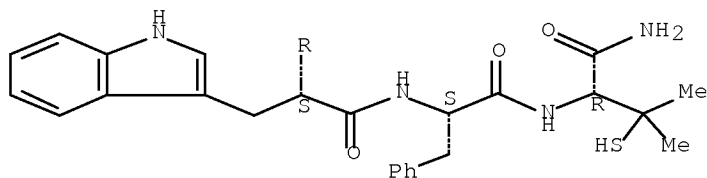


RN 197392-30-6 HCAPLUS

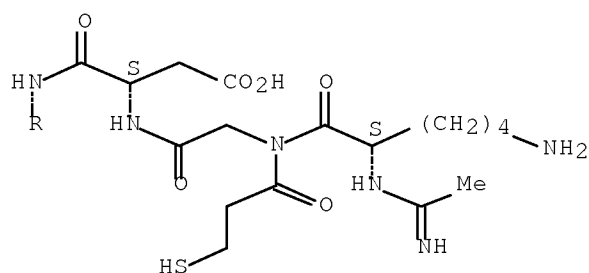
CN L-Valinamide, N2-(1-iminoethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



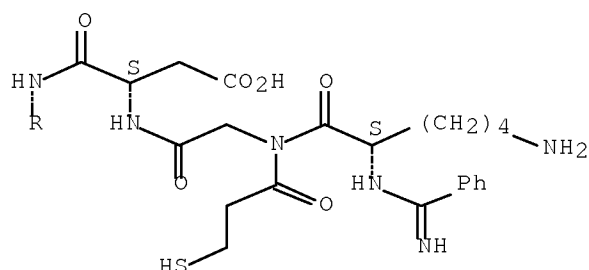
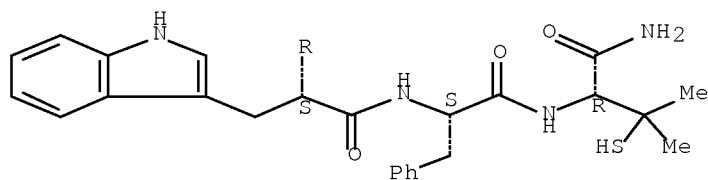
PAGE 2-A



RN 197392-31-7 HCAPLUS

CN L-Valinamide, N2-(iminophenylmethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl-3-mercapto- (9CI) (CA INDEX NAME)

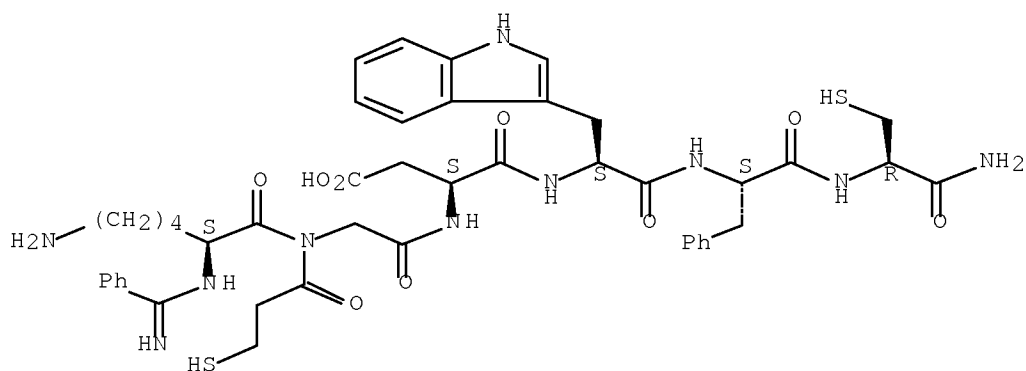
Absolute stereochemistry.



RN 197392-32-8 HCAPLUS

CN L-Cysteinamide, N2-(iminophenylmethyl)-L-lysyl-N-(3-mercapto-1-oxopropyl)glycyl-L- $\alpha$ -aspartyl-L-tryptophyl-L-phenylalanyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-44

ICS A61K031-55; A61K031-395; A61K031-415; A61K031-445; A61K031-495

CC 1-8 (Pharmacology)

Section cross-reference(s): 63

IT 144494-65-5, Tirofiban 155415-08-0 169237-80-3 197392-29-3

197392-30-6 197392-31-7 197392-32-8

197392-33-9 197392-34-0 197392-35-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(method for inhibiting platelet aggregation and clot formation)

L9 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1988:172491 HCAPLUS Full-text  
DOCUMENT NUMBER: 108:172491  
TITLE: Preparation of superplasticizer additive for concrete  
INVENTOR(S): Gusatu, Nicolae; Maurer, Ewald Viliam; Bab, Corneliu  
Ion; Jebelean, Eugen; Ilca, Anita Ileana; Marinescu,  
Vasile; Koreck, Ioan Antoniu  
PATENT ASSIGNEE(S): Intreprinderea de Detergenti, Timisoara, Rom.  
SOURCE: Rom., 3 pp.  
CODEN: RUXXA3  
DOCUMENT TYPE: Patent  
LANGUAGE: Romanian  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RO 91423	B1	19870430	RO 1985-117760	19850226
RITY APPLN. INFO.:			RO 1985-117760	19850226

PRIORITY APPLN. INFO.:

ED Entered STN: 13 May 1988

AB The superplasticizer for concrete consists of 25-50% of a mixture containing 1 mol  $\text{H}_2\text{NCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{N}[\text{COCH}_2\text{CH}(\text{SO}_3\text{Na})\text{CO}_2\text{Na}]\text{CH}_2\text{CH}_2\text{NHCOCH}_2\text{CH}(\text{SO}_3\text{Na})\text{CO}_2\text{Na}$  or  $\text{H}_2\text{NCH}_2\text{CH}_2\text{N}[\text{COCH}_2(\text{SO}_3\text{Na})\text{CO}_2\text{Na}]\text{CH}_2\text{CH}_2\text{N}[\text{COCH}_2\text{CH}(\text{SO}_3\text{Na})\text{CO}_2\text{Na}]\text{CH}_2\text{CH}_2\text{NHCOCH}_2\text{CH}(\text{SO}_3\text{Na})\text{CO}_2\text{Na}$  and 1-2 mol  $\text{ROOCH}_2\text{CH}(\text{SO}_3\text{Na})\text{CO}_2\text{Na}$  (where R = C4-8 alkyl) and 50-75% water. Triethylenetetramine (I) is reacted with .apprx.0.5 h with monoester of maleic acid and C4-8 alc. at a mol. ratio of 1:(1-2) and 50-60°. The reaction product is treated .apprx.1 h with maleic anhydride at a I/maleic anhydride mol ratio of 1:(2-3) at 90-100°, and the obtained product is treated 1-2 h with a  $\text{Na}_2\text{SO}_3$  solution at a I/ $\text{Na}_2\text{SO}_3$  mol ratio of 1:(2-4) at 60-70° to give the title superplasticizer. Thus, I 146 g was reacted 0.5 h with 2-ethylhexyl monoester of maleic acid 456 g at 50-60°, and maleic anhydride 196 g was added. The exothermic reaction was completed in 1 h at 90-100°. Then, 1300 g water was added, the reaction mixture was cooled to 60-70°, 504 g  $\text{Na}_2\text{SO}_3$  was added with stirring, and the reaction was continued 1-2 h at 60-70°. The reaction was finished when the  $\text{Na}_2\text{SO}_3$  content decreased below 0.5%.

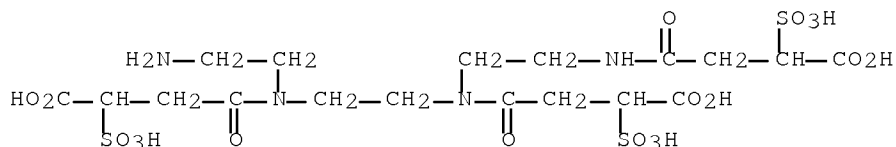
IT 113900-54-2

RL: USES (Uses)

(superplasticizers, for concrete)

RN 113900-54-2 HCAPLUS

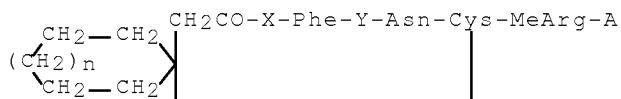
CN Butanoic acid, 4-[[2-[(2-aminoethyl)(3-carboxy-1-oxo-3-sulfopropyl)amino]ethyl][2-[(3-carboxy-1-oxo-3-sulfopropyl)amino]ethyl]amino]-4-oxo-2-sulfo-, hexasodium salt (9CI) (CA INDEX NAME)



IC ICM C04B024-02  
ICS C04B026-20  
CC 58-2 (Cement, Concrete, and Related Building Materials)  
IT 108-31-6D, reaction products with ethylhexyl maleate and triethylenetetramine, sulfonated, sodium salts 112-24-3D, reaction products with ethylhexyl maleate and maleic anhydride, sulfonated, sodium salts 7423-42-9D, 2-Ethylhexyl maleate, reaction products with maleic anhydride and triethylenetetramine, sulfonated, sodium salts 113900-54-2 113900-55-3  
RL: USES (Uses)  
(superplasticizers, for concrete)

L9 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 1987:618079 HCAPLUS Full-text  
DOCUMENT NUMBER: 107:218079  
TITLE: Preparation of vasopressin antagonists for treatment of hypertension, congestive heart failure, and hepatic cirrhosis  
INVENTOR(S): Ali, Fadia Elfehail; Marshall, Garland Ross; Huffman, William Francis; Moore, Michael Lee  
PATENT ASSIGNEE(S): SmithKline Beckman Corp., USA  
SOURCE: Eur. Pat. Appl., 12 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 225109	A2	19870610	EP 1986-308981	19861118
EP 225109	A3	19890607		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4687758	A	19870818	US 1985-799718	19851119
ZA 8608690	A	19870826	ZA 1986-8690	19861117
JP 62155298	A	19870710	JP 1986-275088	19861118
DK 8605539	A	19870520	DK 1986-5539	19861119
AU 8665383	A	19870521	AU 1986-65383	19861119
AU 595258	B2	19900329		
PRIORITY APPLN. INFO.:			US 1985-799718	A 19851119
ED Entered STN: 12 Dec 1987				
GI				



I

AB The title compds. [I; A = NH<sub>2</sub>, OH, Gly-OH, Gly-NH<sub>2</sub>, or a salt, ester, or N-alkylamide thereof; X = D or L-Tyr, Tyr(alkyl), Ile, Phe, Phe(alkyl); Y = Val, Abu; Abu =  $\alpha$ -aminobutyric acid; n = 0, 1] are vasopressin antagonists and are useful for treatment of hypertension, congestive heart failure, and hepatic cirrhosis. I (A = NH<sub>2</sub>, X = D-Tyr(Et), Y = Val, n = 1) (II) was prepared by

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the solid-phase method on benzhydrylamine resin using tert-butoxycarbonyl-protected amino acids followed by resin cleavage using HF and disulfide bond formation using K<sub>3</sub>Fe(CN)<sub>6</sub> in aqueous HOAc. II at 24.5 µg/kg in rats reduced urine osmolality to 300 m-Osmoles/kg.

IT 111230-81-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

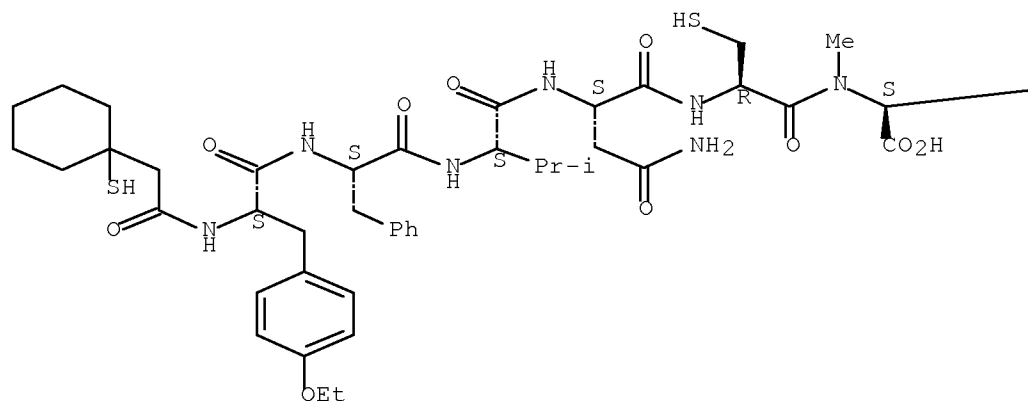
(preparation and disulfide bond formation of, in preparation of vasopressin antagonist)

RN 111230-81-0 HCAPLUS

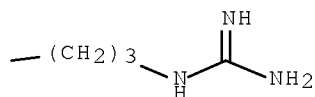
CN L-Arginine, N2-[N-[N2-[N-[N-[O-ethyl-N-[(1-mercaptocyclohexyl)acetyl]-L-tyrosyl]-L-phenylalanyl]-L-valyl]-L-asparaginyl]-L-cysteinyl]-N2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IC ICM C07K007-06

ICS C07K007-16; A61K037-64

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

IT 111230-78-5P 111230-79-6P 111230-81-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and disulfide bond formation of, in preparation of vasopressin antagonist)

L9 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1987:499253 HCAPLUS Full-text

DOCUMENT NUMBER: 107:99253  
 TITLE: A process for the froth-flotation of a phosphate mineral, and a reagent intended for use in the process  
 INVENTOR(S): Weckman, Anders; Anders, Weckman; Kari, Esko Tapio; Esko, Tapio Kari; Aaltonen, Jarmo; Jarmo, Aaltonen  
 PATENT ASSIGNEE(S): Kemira Oy, Finland  
 SOURCE: S. African, 28 pp.  
 CODEN: SFXXAB  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 8602450	A	19861126	ZA 1986-2450	19860403
FI 8403992	A	19860412	FI 1984-3992	19841011
FI 8503942	A	19860412	FI 1985-3942	19851010
FI 72899	B	19870430		
FI 72899	C	19870810		
AU 8655646	A	19870416	AU 1986-55646	19860404
AU 594948	B2	19900322		
IN 167219	A1	19900922	IN 1986-MA266	19860410
CN 86102467	A	19870408	CN 1986-102467	19860411
CN 1009345	B	19900829		
BR 8601645	A	19870602	BR 1986-1645	19860411
US 4755285	A	19880705	US 1986-850814	19860411
SU 1480754	A3	19890515	SU 1986-4027345	19860411
PRIORITY APPLN. INFO.:			FI 1985-3942	A 19851010
			FI 1984-3992	A 19841011

ED Entered STN: 19 Sep 1987

AB The title process, especially suitable for phosphate-carbonate ores, employs a selective reagent of general formula  $(\text{HO}_2\text{CXCO})_m[\text{N}(\text{R}_1)\text{YCO}]_n\text{B}$  ( $\text{X} = \text{CH}:\text{CH}$ ,  $\text{C}(\text{NRR}_3)\text{HCH}_2$ , or  $\text{C}(\text{SO}_3\text{H})\text{HCH}_2$ ;  $\text{Y} = \text{C}(\text{CO}_2\text{H})\text{HCH}_2$  or  $\text{CH}(\text{CH}_2\text{CO}_2\text{H})$ ;  $n = 0-40$ ;  $m = 0, 1$ ;  $\text{B} = \text{NRR}_2$  or a cyclic group;  $\text{R} = \text{H}$ ,  $\text{R}_3$  or a cyclic group;  $\text{R}_1-3 = \text{C}_1-30$  hydrocarbyl). An ore containing fluorapatite 9.6, carbonates 9.0%, and balance silicate, was crushed, and mixed with water to give a slurry containing 36.3% <74- $\mu$  material. A compound of formula  $\text{HO}_2\text{CCH}:\text{CHCO}[\text{N}(\text{R}_4)\text{C}(\text{CO}_2\text{H})\text{HCH}_2\text{CO}]_{10}\text{NR}_4\text{H}$  ( $\text{R}_4 = \text{C}_3\text{H}_6\text{OC}_8\text{H}_{17}$ ) was added at 200 g/ton to the slurry, and, in 4 flotation steps, apatite concentrate was obtained in 93.2% yield, containing 30.6%  $\text{P}_2\text{O}_5$ , vs. 4.0% in the original ore.

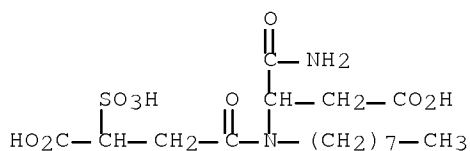
IT ~~110008-34-9D~~, C16-18-alkyl derivs.

RL: USES (Uses)

(flotation agent, in phosphate ore concentration)

RN 110008-34-9 HCAPLUS

CN Butanoic acid, 4-[[2-amino-1-(carboxymethyl)-2-oxoethyl]octylamino]-4-oxo-2-sulfo-, monosodium salt (9CI) (CA INDEX NAME)

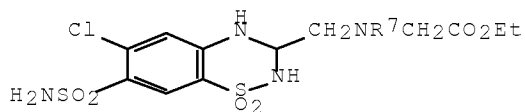


● Na

IC ICM B03D  
 CC 49-9 (Industrial Inorganic Chemicals)  
 IT 541-59-3D, C16-18-alkyl derivs. 4452-01-1D, C16-18-alkyl derivs.  
 60387-06-6 93804-04-7 100581-97-3 110008-24-7D, C16-18-alkyl derivs.  
 110008-25-8D, C16-18-alkyl derivs. 110008-26-9D, C16-18-alkyl derivs.  
 110008-27-0 110008-28-1 110008-29-2 110008-30-5 110008-31-6  
 110008-32-7 110008-33-8 110008-34-9D, C16-18-alkyl derivs.  
 110018-29-6 110018-30-9 110022-67-8 110041-94-6 110044-20-7D,  
 maleoyl-terminated 110044-21-8D, maleoyl-terminated 110118-98-4  
 RL: USES (Uses)  
 (flotation agent, in phosphate ore concentration)

L9 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1986:110168 HCAPLUS Full-text  
 DOCUMENT NUMBER: 104:110168  
 ORIGINAL REFERENCE NO.: 104:17481a,17484a  
 TITLE: N-(benzothiadiazinylalkyl)glycines for treating  
 hypertension  
 INVENTOR(S): Suh, John T.; Piwinski, John J.; Jones, Howard; Neiss,  
 Edward S.  
 PATENT ASSIGNEE(S): USV Pharmaceutical Corp., USA  
 SOURCE: Eur. Pat. Appl., 22 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 153755	A2	19850904	EP 1985-102266	19850228
EP 153755	A3	19860416		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4576941	A	19860318	US 1984-584576	19840229
AU 8539284	A	19850905	AU 1985-39284	19850228
AU 576350	B2	19880825		
JP 60208955	A	19851021	JP 1985-37790	19850228
ES 541341	A1	19851216	ES 1985-541341	19850228
US 4696939	A	19870929	US 1985-802921	19851129
PRIORITY APPLN. INFO.:			US 1984-584576	A 19840229
OTHER SOURCE(S): MARPAT 104:110168				
ED Entered STN: 05 Apr 1986				
GI				



I

AB Amino acids  $RS(CH_2)_nCR_1R_2CON(Z_1R_6)CR_3R_4COR_5$  ( $R = H$ , acyl;  $R_1-R_4 = H$ , hydrocarbyl, aminoalkyl;  $R_5 = OH$ , esterified OH, amino;  $Z_1 =$  alkylene, heteroalkylene;  $R_6 =$  aryl, fused polycyclic aryl, heteroaryl, benzoheterocyclyl;  $n = 0-3$ ; ), useful as antihypertensives, were prepared

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(Benzothiadiazinylmethyl)glycine I·HCl (R7 = H) was treated with AcSCH<sub>2</sub>CHMeCO<sub>2</sub>H, N,N'-carbonyldiimidazole, and Et<sub>3</sub>N to give I (R7 = AcSCH<sub>2</sub>CHMeCO).

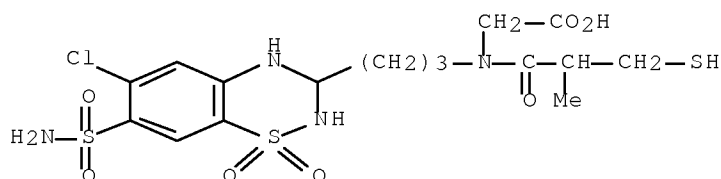
IT 100821-55-4P 100821-62-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as antihypertensive)

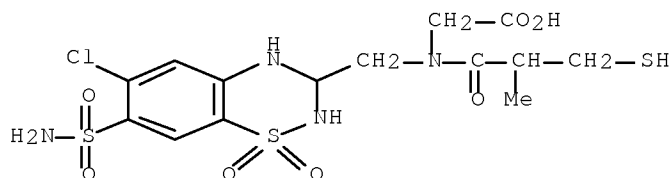
RN 100821-55-4 HCAPLUS

CN Glycine, N-[3-[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]propyl]-N-(3-mercapto-2-methyl-1-oxopropyl)- (CA INDEX NAME)



RN 100821-62-3 HCAPLUS

CN Glycine, N-[[7-(aminosulfonyl)-6-chloro-3,4-dihydro-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl]methyl]-N-(3-mercapto-2-methyl-1-oxopropyl)- (CA INDEX NAME)



IC ICM C07D285-30

ICS C07D285-14; C07D239-90; C07D231-56; A61K031-54; A61K031-41; A61K031-505

ICA C07C101-04

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 28

IT 100821-52-1P 100821-53-2P 100821-55-4P 100821-56-5P

100821-57-6P 100821-58-7P 100821-59-8P 100821-60-1P 100821-61-2P

100821-62-3P 100843-89-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as antihypertensive)



10/537000

\*\*\*\*\* SEARCH HISTORY \*\*\*\*\*

=> d his nofile

(FILE 'HOME' ENTERED AT 16:05:55 ON 19 MAR 2008)

FILE 'HCAPLUS' ENTERED AT 16:06:04 ON 19 MAR 2008

L1 1 SEA ABB=ON PLU=ON US20060160086/PN  
D IBIB AB IT SC

FILE 'REGISTRY' ENTERED AT 16:57:47 ON 19 MAR 2008

L2 STRUCTURE UPLOADED  
D

L3 3 SEA SSS SAM L2  
D SCAN

L4 64 SEA SSS FUL L2  
SAVE TEMP L4 MUM000REGL1/A

FILE 'STNGUIDE' ENTERED AT 16:59:52 ON 19 MAR 2008

FILE 'REGISTRY' ENTERED AT 17:04:52 ON 19 MAR 2008

L5 STRUCTURE UPLOADED  
D

L6 STRUCTURE UPLOADED  
D

L7 2 SEA SUB=L4 SSS SAM (L5 OR L6)  
D SCAN

L8 14 SEA SUB=L4 SSS FUL (L5 OR L6)  
D SCAN  
SAVE TEMP L8 MUM000REGL34/A

FILE 'HCAPLUS' ENTERED AT 17:08:33 ON 19 MAR 2008

L9 8 SEA ABB=ON PLU=ON L8

L10 1 SEA ABB=ON PLU=ON L9 AND L1  
D SCAN L9 TI HIT

L11 35 SEA ABB=ON PLU=ON L4

L12 1 SEA ABB=ON PLU=ON L11 AND 80/SC, SX  
D SCAN  
SAVE TEMP L9 MUM000HCAP/A

L13 51 SEA ABB=ON PLU=ON VOLLAND H?/AU

L14 190 SEA ABB=ON PLU=ON CREMINON C?/AU

L15 3 SEA ABB=ON PLU=ON NEUBURGER L?/AU

L16 274 SEA ABB=ON PLU=ON GRASSI J?/AU

L17 1 SEA ABB=ON PLU=ON (((L13 OR L14 OR L15 OR L16)) AND L9) OR  
(L1 AND L9)

FILE 'REGISTRY' ENTERED AT 17:14:13 ON 19 MAR 2008

L18 0 SEA ABB=ON PLU=ON L4 AND (BIOSIS/LC OR BIOTECHNO/LC OR  
SCISEARCH/LC)

FILE 'BIOSIS, BIOTECHNO, PASCAL, SCISEARCH' ENTERED AT 17:15:03 ON 19 MAR  
2008

L19 40 SEA ABB=ON PLU=ON L13 AND ((L14 OR L15 OR L16))

L20 239 SEA ABB=ON PLU=ON L14 AND (L15 OR L16)

L21 2 SEA ABB=ON PLU=ON L15 AND L16

L22 250 SEA ABB=ON PLU=ON (L19 OR L20 OR L21)

L23 42 SEA ABB=ON PLU=ON L22 AND (ANALYT? OR TRIFUNCT? OR DETECT?  
REAGENT?)

L24 0 SEA ABB=ON PLU=ON L23 AND (CONTINU? DETECT?)  
D TI AU L21 1-2

10/537000

L25            2 SEA ABB=ON PLU=ON L23 AND FLUORES?  
L26           11 SEA ABB=ON PLU=ON L23 AND SOLID PHASE?  
              D L26 TI AU 1-5  
L27           11 SEA ABB=ON PLU=ON L25 OR L26  
              SAVE TEMP L27 MUM000MULTIN/A

FILE 'STNGUIDE' ENTERED AT 17:20:25 ON 19 MAR 2008  
D QUE L17

FILE 'HCAPLUS, BIOSIS, BIOTECHNO, PASCAL, SCISEARCH' ENTERED AT 17:21:21  
ON 19 MAR 2008

L28           9 DUP REM L17 L27 (3 DUPLICATES REMOVED)  
              ANSWER '1' FROM FILE HCAPLUS  
              ANSWERS '2-7' FROM FILE BIOSIS  
              ANSWERS '8-9' FROM FILE PASCAL  
D L28 1 IBIB ABS HITSTR  
D L28 IBIB AB 2-9  
D QUE L9  
D L9 1-8 IBIB ED ABS HITSTR HITIND